Letter to editor

Is increased lactate during exercise dangerous for cancer patients: An editorial

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Dear Editor-in-Chief

Lactate can be a key factor in cancer tumor progression

One of the clear indicators of cancerous tumors is an uneven distribution of oxygen, resulting in the presence of both hypoxic and normoxic areas within the tumor (Goodwin et al., 2015). Consequently, these conditions can contribute to the acidity of the tumor environment (Goodwin et al., 2015). The significant increase in lactate levels observed in cancerous tumors is primarily attributed to the heightened activity of the glycolysis cycle (Goodwin et al., 2015), a phenomenon identified by Otto Warburg in 1927, known as the Warburg effect (Pérez-Tomás & Pérez-Guillén, 2020). Despite the common misconception that lactate is a waste molecule, emerging evidence suggests that lactate may actually play a role in promoting cancer progression, particularly in support of cancer cells (Lavín-Pérez et al., 2023; Pérez-Tomás & Pérez-Guillén, 2020). Therefore, there is strong evidence to support the notion that lactate serves as the primary fuel to fulfill the anabolic requirements of cancer cells, potentially serving as a key factor in cancer growth (Lavín-Pérez et al., 2023; Pérez-Tomás & Pérez-Guillén, 2020). Given the complex physiological conditions associated with cancer, it raises the question of whether exercise is appropriate for cancer patients or not.

Lactate, exercise, and cancer

Considering these complex physiological conditions, whether exercise in cancer patients can be appropriate (Lavín-Pérez et al., 2023). Several studies have investigated the effect of exercise during cancer with different mechanisms that have reported the positive effect of exercise to improve psychological or immunological effects (Lavín-Pérez et al., 2023). However, the special concentration of exercise, lactate, and its relationship with tumor growth has yet to be specifically investigated. Physiologically, exercise with any intensity can increase lactate (Stallknecht et al., 1998). One of the factors that can have a significant effect on increasing lactate is the intensity of training (Stallknecht et al., 1998). According to Brooks et al., lactate is the largest myokine in concentration and dynamic range and the most diverse in metabolic and physiological regulation (Stallknecht et al., 1998). In the past, lactate was believed to be produced in anaerobic conditions. However, in recent years, the theory has been proposed that lactate is also produced in completely aerobic conditions (Stallknecht et al., 1998). Therefore, aerobic and anaerobic training will increase lactate (Stallknecht et al., 1998). As the intensity of training increases, the ratio of NAD+ to NADH increases. As a result, fat oxidation decreases, focuses on the glycolysis cycle, and increases lactate (A factor that can be harmful to cancer (Stallknecht et al., 1998). Also, common research supports the hypothesis that lactate increase during exercise can lead to angiogenesis and is one of the key factors of this process (Ahmadi Hekmatikar et al., 2019; Hubbard, 1973; Khoramipour et al., 2020). It seems that lactate can 1) through its effect on factors such as vascular endothelial growth factor and 2) as an important cardiac fuel and metaboreflex regulation leading to greater cardiac output for angiogenesis. On the other hand, considering that there is hyperlactatemia in cancer and the long history of cancerous tumors absorbing lactate, researchers are looking to prevent lactate transport in tumors by blocking MCTs. Accordingly, the development of therapies that limit lactate exchange and signaling within and between cancer cells should be a priority in cancer research, contrary to the physiological effects of exercise.

Finally, the hypothesis that lactate could be suitable for cancer patients during cancer seems false, given the strong results. Both directly, as an energy source, and indirectly, as a gluconeogenic precursor, lactate plays a major role in the bioenergetics and self-sufficiency of cancer cells. Acutely and chronically, exercise has positive physiological effects that cannot be suitable for cancer patients. On the other hand, the

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tumor environment is such that lactate is one of its key fuels for aggressiveness and growth. On the other hand, lactate itself induces angiogenesis. Physiological changes that occur due to exercise can increase lactate, angiogenesis, and lactate transporters, which can benefit the tumor. Physiological changes that occur due to exercise can increase lactate, angiogenesis, and lactate transporters, which can benefit the tumor. However, this study suggests that researchers should focus on exercise and the effects of lactate on cancerous tumors in future studies.

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